



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Benson et al.

Group Art Unit: 1652

Serial No.: 10/028,224

Examiner: David J. Steadman

Confirmation No.: 4497

Filed: December 21, 2001

Docket No.: 00403.CN1

Title: CRYSTALLIZATION AND STRUCTURE DETERMINATION OF GLYCOSYLATED HUMAN BETA SECRETASE, AN ENZYME IMPLICATED IN ALZHEIMER'S DISEASE

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

We are transmitting the following documents along with this Transmittal Sheet (which is submitted in triplicate):

- ☒ An itemized return postcard.  
☒ A Petition for Extension of Time for 3 month(s) and a check in the amount of \$950 for the required fee.  
☒ An Information Disclosure Statement (2 pgs); copy of 1 application; 1449 form (1 pg); and copies of 3 documents cited on the 1449 form.  
☒ A check in the amount of \$180, for *Information Disclosure Statement fee*.  
☒ Other: Amendment and Response (33 pgs); Exhibit A (7 pgs); and copies of documents listed on Exhibit A (87 documents total).  
Amendment ☐ No Additional fee is required. ☐ The fee has been calculated as shown:

Fee Calculation for Claims Pending After Amendment					
	Pending Claims after Amendment (1)	Claims Paid for Earlier (2)	Number of Additional Claims (1-2)	Cost per Additional Claim	Additional Fees Required
Total Claims				x \$18 =	
Independent Claims				x \$86 =	
One or More New Multiple Dependent Claims Presented? If Yes, Add \$290 Here →					
Total Additional Claim Fees Required					

Please consider this a PETITION FOR EXTENSION OF TIME for a sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 13-4895. Triplicate copies of this sheet are enclosed.

MUETING, RAASCH & GEBHARDT, P.A.

Customer Number: 26813

By: 

Name: Loren D. Albin

Reg. No.: 37,763

Direct Dial: 612-305-1225

Facsimile: 612-305-1228

CERTIFICATE UNDER 37 CFR §1.10:

"Express Mail" mailing label number: EV 073687877 US

Date of Deposit: FEBRUARY 12, 2004

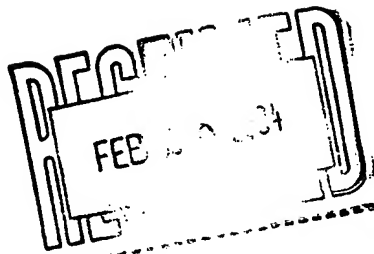
I hereby certify that the Transmittal Letter and the paper(s) and/or fee(s), as described hereinabove, are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By: 

Name: SAM HER

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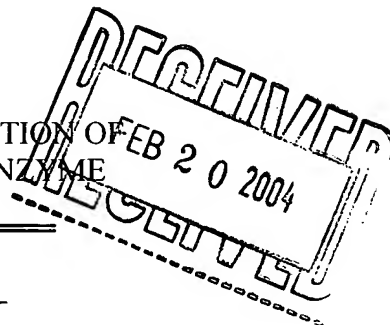
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PATENT  
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	)		
Serial No.: 10/028,224	)	Examiner:	David J. Steadman
Confirmation No.: 4497	)		
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For:		CRYSTALLIZATION AND STRUCTURE DETERMINATION OF	
		GLYCOSYLATED HUMAN BETA SECRETASE, AN ENZYME	
		<u>IMPLICATED IN ALZHEIMER'S DISEASE</u>	



INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450 (via Express Mail)

Sir:

In accordance with the continuing duty of candor and good faith that is to be demonstrated before the United States Patent and Trademark Office (USPTO), enclosed are copies of documents which Applicants bring to the Examiner's attention as possibly being of interest in connection with the above-identified patent application. Per M.P.E.P. § 609, the information cited in the present Information Disclosure Statement shall not be construed to be an admission that the information is, or is considered to be, material to patentability. Consideration of each of the documents listed on the attached 1449 form(s) is respectfully requested. Pursuant to the provisions of MPEP §609, Applicants further request that a copy of the 1449 form(s), marked as being considered and initialed by the Examiner, be returned with the next Official Communication.

Applicants also wish to bring the Examiner's attention to the following pending U.S. Application, as well as any documents, Office Actions that may include rejections of similar claims, and any provisional U.S. patent applications referenced therein. A copy of the below-listed pending U.S. Patent Application is provided herewith.

**Information Disclosure Statement**

Page 2 of 2

Applicant(s): Benson et al.

Serial No.: 10/028,224

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For: CRYSTALLIZATION AND STRUCTURE DETERMINATION OF GLYCOSYLATED HUMAN BETA SECRETASE, AN ENZYME IMPLICATED IN ALZHEIMER'S DISEASE

**List of Pending Non-Published U.S. Patent Applications**

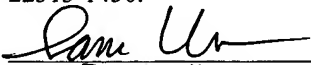
Applicant(s)	Application Number	Filing Date	Serial No. of Provisional Application to which listed Application claims priority
Benson et al.	10/435,533	05/09/03	60/379,690

Since this Information Disclosure Statement is submitted after the receipt of an Office Action in the above-identified patent application, Applicants have included the fee of \$180 under 37 C.F.R. §§1.97(c) and 1.17(p). Please charge any additional fees or credit any overpayment to Deposit Account No. 13-4895.

When the Examiner takes up the present application, consideration of these documents is respectfully requested. The Examiner is invited to contact Applicants' Representatives at the below-listed telephone number, if they can be of any assistance during prosecution of the present application.

**CERTIFICATE UNDER 37 C.F.R. 1.10:**

The undersigned hereby certifies that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



Name: SAM HER  
"Express Mail" mailing label number:  
EV 073687877 US  
Date of Deposit: **FEBRUARY 12, 2004**

Respectfully submitted for

**Benson et al.**

By

Muetting, Raasch &amp; Gebhardt, P.A.

P.O. Box 581415

Minneapolis, MN 55458-1415

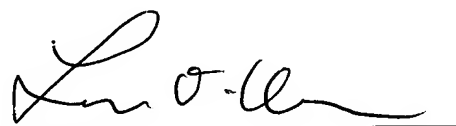
Telephone (612)305-1220

Facsimile (612)305-1228

**Customer Number 26813**

February 12, 2004  
Date

By:



Loren D. Albin

Reg. No. 37,763

Direct Dial (612)305-1225

**INFORMATION  
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Atty. Docket No.: 00403.CN1

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Application Filing Date: Dec. 21, 2001

Group: 1652

Information Disclosure Statement mailed: **FEBRUARY 12, 2003**

via Express Mail No. EV 073687877 US

**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
	2003/0095958 A1	05/22/03	Bhissetti et al.			

**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No
	NONE						

**OTHER DOCUMENTS (Including Authors, Title, Date, Pertinent Papers, etc.)**

Examiner Initial	Document Description
	Drenth, "Principles of Protein X-ray Crystallography," Second Edition, 1994 Springer-Verlag New York, Inc., pages 1-18.

**EXAMINER****Date Considered**

\*Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**INFORMATION  
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Atty. Docket No.: 00403.CN1

Serial No.: 10/028,224

Applicant(s): T. E. Benson et al.

Confirmation No.: unknown

Filing Date: December 21, 2001

Group: unknown

**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
	6,221,645 B1	04/24/01	Chrysler et al.			
	6,225,103 B1	05/01/01	Keolsch et al.			
	6,245,884 B1	06/12/01	Hook			
	6,258,386 B1	06/10/01	Xia et al.			
	6,268,158 B1	07/31/01	Pantoliano et al.			
	2001/0016324 A1	08/23/01	Gurney et al.			
	2001/0018208 A1	08/30/01	Gurney et al.			
	2001/0021391 A1	09/13/01	Gurney et al.			
	6,291,223 B1	09/18/01	Christie et al.			
	6,329,163 B1	12/11/01	Anderson et al.			

**FOREIGN PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No
	WO 01/00663 A2	01/04/01	PCT				
	WO 01/00665 A2	01/04/01	PCT				
	WO 01/23533 A2	04/05/01	PCT				
	WO 01/49098 A2	07/12/01	PCT				
	WO 01/50829 A2	07/19/01	PCT				

**OTHER DOCUMENTS (Including Authors, Title, Date, Pertinent Papers, etc.)**

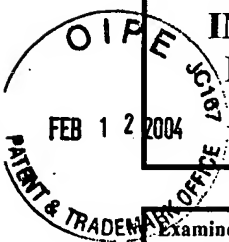
Examiner Initial	Document Description
	Bartlett et al., "CAVEAT: A program to facilitate the structure-derived design of biologically active molecules," <i>Molecular Recognition: Chemical and Biological Problems</i> , Royal Society of Chemistry, Special Pub No. 78:182-196 (1989).
	Benson et al., "An enzyme-substrate complex involved in bacterial cell wall biosynthesis," <i>Nat Struct Biol.</i> 1995 Aug;2(8):644-53.

EXAMINER

Date Considered

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EXHIBIT A

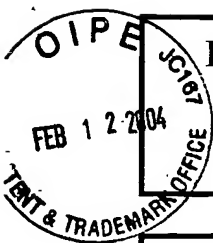


<b>INFORMATION DISCLOSURE STATEMENT</b>	<b>Atty. Docket No.:</b> 00403.CN1	<b>Serial No.:</b> 10/028,224
	<b>Applicant(s):</b> T. E. Benson et al.	<b>Confirmation No.:</b> unknown
	<b>Filing Date:</b> December 21, 2001	<b>Group:</b> unknown

Examiner Initial	Document Description
	Berman et al., "The Protein Data Bank," <i>Nucleic Acids Res.</i> 2000 Jan 1;28(1):235-42.
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	Haniu et al., "Characterization of Alzheimer's beta -secretase protein BACE. A pepsin family member with unusual properties," <i>J Biol Chem.</i> 2000 Jul 14;275(28):21099-106.
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<p>*Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

EXHIBIT A


**INFORMATION  
DISCLOSURE  
STATEMENT**

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Serial No.: 10/028,224

Applicant(s): T. E. Benson et al.

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Group: unknown

Examiner Initial	Document Description
	Hong et al., "Structure of the protease domain of memapsin 2 ( $\beta$ -secretase) complexed with inhibitor," <i>Science</i> . 2000 Oct 6;290(5489):150-3.
	Huang et al., "A 3D-structural model of memapsin 2 protease generated from theoretical study," <i>Acta Pharmacol Sin</i> . 2001 Jan;22(1):50-56.
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	National Institutes of Health, "BLAST 2 Sequences," [online] United States; retrieved August 29, 2001 from the Internet: <URL:http://www.ncbi.nlm.nih.gov/gorf/bl2.html>, 1 pg.
	Navaza, "AMoRe: an automated package for molecular replacement," <i>Acta Cryst.</i> 1994;450:157-163.
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	Sack, "CHAIN - A Crystallographic Modeling Program," <i>J Molecular Graphics</i> . 1988 Dec; 6(4):224-5.
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Examiner Initial	Document Description
	Sinha et al. "Purification and cloning of amyloid precursor protein $\beta$ -secretase from human brain," <i>Nature</i> . 1999 Dec 2;402(6761):537-40.
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	Wyckoff et al., eds., <i>Methods in Enzymology Vol. 115. Diffraction Methods for Biological Macromolecules</i> , Academic Press, Orlando, FL; title page, publication page, and table of contents only, 4 pages (1985).
	Yan et al. (1999), "Membrane-anchored aspartyl protease with Alzheimer's disease $\beta$ -secretase activity," <i>Nature</i> . 1999 Dec 2;402(6761):533-7.

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	Applicant(s): Benson et al.	Confirmation No.: 4497
	Application Filing Date: Dec. 21, 2001	Group: 1632
	Information Disclosure Statement mailed: <i>September 9, 2002</i>	

## U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
	5,744,346	04/28/98	Chrysler et al.			
	5,942,400	08/24/99	Anderson et al.			
	6,297,021 B1	10/02/01	Nienaber et al.			
	6,420,534 B1	07/16/02	Gurney et al.			
	6,440,698 B1	08/27/02	Gurney et al.			
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	2002/0081634 A1	06/27/02	Gurney et al.			
	2002/0115600 A1	08/22/02	Koelsch et al.			

## FOREIGN PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No
	WO 01/17369 A2	03/30/00	PCT				
	WO 01/49097 A2	07/12/01	PCT				
	WO 02/053594 A2	07/11/02	PCT				
	WO 02/25276 A1	03/28/02	PCT				

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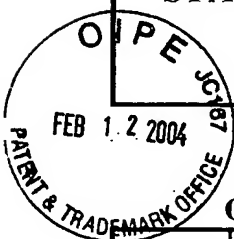
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Group: 1632

Information Disclosure Statement mailed:

Sept. 9, 2002

**OTHER DOCUMENTS (Including Authors, Title, Date, Pertinent Papers, etc.)**

Examiner Initial	Document Description
	Brünger, "X-PLOR: Version 3.1, a System for X-Ray Crystallography and NMR", Yale University Press, New Haven & London, 1992; cover page, publication page and table of contents: 13 pages.
	Brünger et al., "Slow-cooling protocols for crystallographic refinement by simulated annealing," <i>Acta Crystallogr A</i> . 1990 Jul 1;46( Pt 7):585-93.
	"CNX: Crystallography and NMR eXplorer" datasheet, Accelrys Corporate Headquarters, San Diego, CA (2001). [ retrieved August 30, 2002 from the Internet: <URL: <a href="http://www.accelrys.com">http://www.accelrys.com</a> >; 2 pgs.]
	Epps et al., "The ligand affinity of proteins measured by isothermal denaturation kinetics," <i>Anal Biochem</i> . 2001 May 1;292(1):40-50.
	Otwinowski, "Maximum Likelihood Refinement of Heavy Atom Parameters," <i>Isomorphous Replacement and Anomalous Scattering</i> , Wolf et al., eds., Science & Engineering Research Council, Daresbury Laboratory, Warrington, U.K., Proceedings of the CCP4 Study Weekend, 25-26 Jan. 1991; pages 80-86.
	Research Collaboratory for Structural Bioinformatics, "Protein Data Bank," [online] United States; retrieved August 30, 2002 from the Internet: <URL: <a href="http://www.rcsb.org/pdb/">http://www.rcsb.org/pdb/</a> > 8 pages.

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